INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/18848

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07H 21/04
US CL : 536/24.5
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	ELBASHIR et al. RNA interference is mediated by 21 and 22-nucleotide RNAs. Genes and Development. 2001, Vol., 15, pp. 188-200 (see in particular figures 4 and 5; page 195, col. 1; page 198, col. 1).	1, 10-11, 15-18 --- 3-7
X	ELBASHIR et al. Functional anatomy of siRNAs for mediationg efficient RNAi in Drosophila melanogaster embryo lysate. The EMBO Journal. 2001, Vol. 20, No. 23, pp. 6877-6888. see entire document.	1, 3-7 and 10-18

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
02 May 2005 (02.05.2005)

Date of mailing of the international search report
02 AUG 2005

Name and mailing address of the ISA/US
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Form PCT/ISA/210 (second sheet) (January 2004)

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 37-43
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1,3-7 and 10-18

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

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This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) claims 1, 3-7, 10-18, drawn to a double stranded ribonucleic acid (dsRNA) that comprises first and second double stranded ends wherein only one double stranded end comprises a nucleotide overhang of 1-4 unpaired nucleotides, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises a purine and wherein the terminal base pairs at each double stranded end comprise a G-C base pair or wherein the terminal 4 base pairs at each double stranded end comprise at least 2 G-C base pairs.

Group 2, claim(s) 2-4, 8-18, drawn to a dsRNA that comprises first and second double stranded ends wherein the double stranded ends independently comprise a nucleotide overhang of 1-4 unpaired nucleotides, wherein the terminal overhang on at least one end is 5'-GC-3' and wherein the terminal base pairs at each double stranded end comprise a G-C base pair or wherein the terminal 4 base pairs at each double stranded end comprise at least 2 G-C base pairs.

Group 3, claim(s) 19, 21-25 and 28-36, drawn to a method for targeted selection of a dsRNA wherein the dsRNA is a dsRNA as set forth in group 1.

Group 4, claim(s) 20-22 and 26-36, drawn to a method for targeted selection of a dsRNA wherein the dsRNA is a dsRNA as set forth in group 2.

Groups 5-105, claim(s) 38-43, drawn to a method of inhibiting the expression of a target gene in a cell comprising introducing into the cell the dsRNA of group 1 for a time sufficient to obtain degradation of a target gene wherein the target gene is selected from the group consisting of the 100 genes as listed in claims 40 and 43.

Groups 106-206, claim(s) 38-43, drawn to a method of inhibiting the expression of a target gene in a cell comprising introducing into the cell the dsRNA of group 2 for a time sufficient to obtain degradation of a target gene wherein the target gene is selected from the group consisting of the 100 genes as listed in claims 40 and 43.

The inventions listed as Groups 1-206 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of group 1 is considered to be a double stranded ribonucleic acid (dsRNA) that comprises first and second double stranded ends wherein only one double stranded end comprises a nucleotide overhang of 1-4 unpaired nucleotides, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises a purine and wherein the terminal base pairs at each double stranded end comprise a G-C base pair or wherein the terminal 4 base pairs at each double stranded end comprise at least 2 G-C base pairs.

However, language of claim 1 specifically states, "wherein only one double stranded end comprises a nucleotide overhang of 1-4 unpaired nucleotides". Neither this language, nor any other language in Claim 1, excludes dsRNAs with nucleotide overhangs of greater than 4 unpaired nucleotides. The following prior Art is applied.

Elbashir et al. 2001 (The EMBO Journal, Vol, 20, No. 23, pp. 6877-6888) disclose a dsRNA wherein one double stranded end comprises a 3 nucleobase overhang and the other double stranded end comprises a 5 nucleobase overhang wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises an adenosine residue and the terminal base pairs at each double stranded end are G-C base pairs.

Therefore, the technical feature linking the inventions of groups 1-206 does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

Additionally, this international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed polynucleotide sequences, the Markush group shall be regarded as being of similar nature when:
(A) all alternatives have a common property or activity and
(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or
(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant methods of using dsRNA to inhibit gene expression in a target cell are considered to be each separate inventions for the following reasons:

The dsRNA sequences required to practice each method do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. The required dsRNA sequences of the instant application each target and modulate expression of different genes, therefore, each required dsRNA sequence behaves in a different way in the context of the claimed invention. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved.

Further, because the instant dsRNA sequences that are required to practice the instant methods of inhibiting gene expression, do not target the same gene, the required dsRNA sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the dsRNA sequences required to practice the methods claimed in the instant application is lacking and each method which targets a different gene using a different and required dsRNA sequence is considered to constitute a special technical feature.

As the polynucleotide sequences of the instant invention are not recited in the first claimed invention, Applicants will obtain a search of the first claimed invention. For every other invention applicants wish to have searched, applicants need to elect the group and pay an additional fee.

As the methods which require dsRNA sequences are recited in the second or subsequent claimed invention, Applicants will need to elect the group and pay the fee to obtain a search of the first method of inhibiting gene expression which targets the first gene listed in the claims encompassed by the second or subsequent group. For every other target sequence in the second/subsequent group that applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

The special technical feature of group 1 is a double stranded ribonucleic acid (dsRNA) that comprises first and second double stranded ends wherein only one double stranded end comprises a nucleotide overhang of 1-4 unpaired nucleotides, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises a purine and wherein the terminal base pairs at each double stranded end comprise a G-C base pair or wherein the terminal 4 base pairs at each double stranded end comprise at least 2 G-C base pairs.

The special technical feature of group 2 is a dsRNA that comprises first and second double stranded ends wherein the double stranded ends independently comprise a nucleotide overhang of 1-4 unpaired nucleotides, wherein the terminal overhang on at least one end is 5'-GC-3' and wherein the terminal base pairs at each double stranded end comprise a G-C base pair or wherein the terminal 4 base pairs at each double stranded end comprise at least 2 G-C base pairs.

The special technical feature of group 3 is a method for targeted selection of a dsRNA wherein the dsRNA is a dsRNA as set forth in group 1.

The special technical feature of group 4 is a method for targeted selection of a dsRNA wherein the dsRNA is a dsRNA as set forth in group 2.

The special technical feature of groups 5-104 is a method of inhibiting the expression of a target gene in a cell comprising introducing into the cell the dsRNA of group 1 for a time sufficient to obtain degradation of a target gene wherein the target gene is selected from the group consisting of the 100 genes as listed in claims 40 and 43.

The special technical feature of groups 105-204 is a method of inhibiting the expression of a target gene in a cell comprising introducing into the cell the dsRNA of group 2 for a time sufficient to obtain degradation of a target gene wherein the target gene is selected from the group consisting of the 100 genes as listed in claims 40 and 43.

Continuation of B. FIELDS SEARCHED Item 3:
EAST; STN (medline, biosis, embase).
siRNA, blunt, dsRNA, RNAi